



**Clean Copy of Replacement Specification Paragraphs
Filed with the Amendment Responding to the
Office Action Dated 20 February 2002**

RECEIVED
JUL 31 2002
TECH CENTER 1600/2900

Please delete the paragraph at page 4, lines 6 to 8, and substitute in place thereof the paragraph amended to read as follows.

The anti-CD18 antibody used in this method can, for example, be a whole antibody, an antibody fragment (e.g. one of a Fv, Fab, Fab', or F(ab')₂ fragment), a chimeric antibody, a humanized antibody, or a fully human antibody.

Please delete the paragraph at page 13, lines 9 to 17, and substitute in place thereof the paragraph amended to read as follows.

For example, anti-CD18 antibody fragments capable of binding to a mammalian CD18 or a portion thereof, including Fv, Fab, Fab' and F(ab')₂ antibody fragments, are encompassed by the invention. Such fragments can be produced by enzymatic cleavage of whole anti-CD18 antibodies or by recombinant techniques, for example. For instance, papain or pepsin cleavage can generate Fab or F(ab')₂ fragments, respectively. Antibodies can also be produced in a variety of truncated forms using antibody genes in which one or more stop codons has been introduced upstream of the natural stop site. For example, a chimeric gene encoding a F(ab')₂ heavy chain portion can be designed to include DNA sequences encoding the CH₁ domain and hinge region of the heavy chain.

Please delete the paragraph at page 18, lines 14 to 28, and substitute in place thereof the paragraph amended to read as follows.

In one embodiment, a functional variant of mammalian CD18 shares at least about 85% sequence identity with the corresponding mammalian CD18 (e.g. human CD18, as described in GenBank accession number NM_000211, or another primate CD18), preferably at least about 90% sequence identity, and more preferably at least about 95% sequence identity with said mammalian CD18. In another embodiment, a functional fusion protein comprises a first moiety which shares at least about 85% sequence identity with the corresponding mammalian CD18, preferably at least about 90% sequence identity, and more preferably at least about 95% sequence identity with the mammalian CD18. Sequence identity can be determined using a suitable program, such as the Blastx program (Version 1.4), using appropriate parameters, such as default parameters set forth at the NCBI web site. In one embodiment, parameters for Blastx search are scoring matrix BLOSUM62, W=3. In another embodiment, a functional variant comprises a nucleic acid which has a sequence which differs from the naturally-occurring nucleic acid molecule but which, due to the degeneracy of the genetic code, encodes mammalian CD18 or a portion or functional variant thereof.

Please delete the paragraph at page 33, line 24, to page 34, line 13, and substitute in place thereof the paragraph amended to read as follows.

The anti-CD18 antibody used in the therapeutic and preventive methods described herein can be any of the types of anti-CD18 antibodies that are described in this disclosure. For example, a whole antibody can be used (e.g. an isolated murine antibody which specifically binds with human CD18). Alternatively, the anti-CD18 antibody can be a fragment of a whole antibody, such as a Fv, Fab, Fab', or F(ab')₂ fragment. The anti-

CD18 antibody can be an antibody isolated from a human, from a non-human mammal, from a non-human vertebrate, from a library of random or synthetic antibodies. Furthermore, the anti-CD18 antibody can be an antibody which comprises segments obtained from different sources (i.e. a chimeric antibody). By way of example, the antibody can have complementarity-determining regions which have the amino acid sequence of the same regions of a murine antibody which binds specifically with CD18; the same antibody can have non-complementarity-determining regions (also designated structural, framework, or constant regions) which have amino acid sequences which are derived from one or more human antibodies or from consensus human antibody sequences. This antibody is also an example of a type of humanized antibody (i.e. an antibody in which at least a part of the antibody is derived from a non-human source, but which has been modified such that at least one other part of the antibody is more nearly like a human antibody in terms of its amino acid sequence). Anti-CD18 antibodies which are humanized, using any of the methods described herein or any other method known in the art or hereafter developed, can be used in any of the methods described in this disclosure.

Please delete the paragraph at page 41, lines 21-28, and substitute in place thereof the paragraph amended to read as follows.

Efficacy of treatment was evaluated by use of quantitative angiography at the time of stent placement and at the end of the study, and by immunohistologic and morphometric evaluation of iliac artery tissue. Blood samples were collected periodically for assay of serum mAb levels (pharmacokinetics), leukocyte mAb binding (pharmacodynamics), anti-mAb antiglobulin response (immunogenicity), and for hematology and serum chemistry (safety). Safety was further evaluated by recording vital signs during infusion and body weights, clinical observations and injection site

observations during the test period. Other tissue samples were not evaluated unless warranted (see Table B).

Please delete the paragraph at page 45, lines 21-26, and substitute in place thereof the paragraph amended to read as follows.

1B4 is a murine IgG2a mAb that recognizes CD18 on human, non-human primate and rabbit neutrophils. 1B4 was produced using a commercially available cell line that makes the antibody (ATCC Accession No. HB-10164). S-S.1 is a murine IgG2a mAb directed against sheep red blood cells. S-S.1 was produced using a commercially available cell line that makes the antibody (ATCC Accession No. TIB-111) and is being used as an irrelevant isotype-matched control antibody.